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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

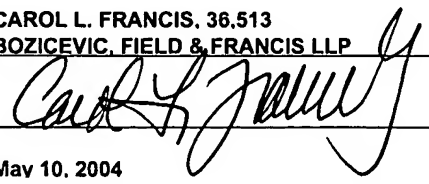
Application Number	10/676,727
Filing Date	September 30, 2003
First Named Inventor	VERKMAN, ALAN
Group Art Unit	1614
Examiner Name	Not Yet Assigned
Total Number of Pages in This Submission: 6	Attorney Docket Number: UCSF-291

ENCLOSURES (check all that apply)

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment / Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☒ **Information Disclosure Statement PTO-SB/08A**
- ☐ Certified Copy of Priority Documents
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☒ Other Enclosure(s) *(please identify below):*
  - **50 References**
  - **Postcard**

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	CAROL L. FRANCIS, 36,513 BOZICEVIC, FIELD & FRANCIS LLP
Signature	
Date	May 10, 2004

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Application Number	10/676,727
Filing Date	September 30, 2003
First Named Inventor	VERKMAN, ALAN
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  PTO-SB/08A
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- ☐ Proprietary Information
- ☒ **MEMORANDUM REGARDING COMPOUND COLLECTIONS (2 pgs.)**
- ☒ Other Enclosure(s) *(please identify below):*
  1 Reference
  Postcard

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	CAROL L. FRANCIS, 36,513 BOZICEVIC, FIELD & FRANCIS LLP
Signature	Carol L. Francis
Date	May 10, 2004

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This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

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Alexandria, VA 22313-1450

Attorney Docket	UCSF-291
First Named Inventor	VERKMAN, ALAN
Application Number	10/676,727
Confirmation No.	2946
Filing Date	September 30, 2003
Group Art Unit	1614
Examiner Name	Unassigned
Title: "CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR PROTEIN INHIBITORS AND USES THEREOF"	

Sir:

This is an Information Disclosure Statement submitted for the Examiner's consideration. A Form PTO-SB/08A listing the references and copies of the cited references accompany this paper. Applicants would appreciate the Examiner's initialing and returning the form to indicate that the references have been reviewed and made of record.

This Information Disclosure Statement is not intended as a representation that a search has been made, that additional information material to the examination of this application does not exist, or that any one of the above references constitutes prior art to the present application within the meaning of 35 U.S.C.§102.

As applicants have not yet received a first Action on the merits, no fee is believed to be required for filing this Disclosure Statement. If, however, the PTO finds that for some reason a fee is due, our Deposit Account No. 50-0815, Order No. UCSF-291 may be charged thereon.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 10, 2004

By: _____
Carol L. Francis
Registration No. 36,513

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200 Middlefield Road, Suite 200
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MEMORANDUM REGARDING COMPOUND COLLECTIONS

Address to:
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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Application Number	10/676,727
Attorney Docket No.	UCSF-291
Confirmation Number	2946
Filing Date	September 30, 2003
First Named Inventor	Alan Verkman
Examiner	Unassigned
Group Art	1614
Title:	"Cystic Fibrosis Transmembrane Conductance Regulator Protein Inhibitors and Uses Thereof"

Sir:

Applicants hereby request that the following be considered and made of record in the above-referenced application.

Identification of some of the compounds having the desired characteristics was accomplished by initialing screening a diverse collection of approximately 50,000 drug-like compounds purchased without obligation of confidentiality from ChemBridge (San Diego, CA) or ChemDiv (San Diego, CA), which compounds were provided in stock solutions of 10 mM DMSO. The compounds identified from this initial screen were:

(1) 3-[(3-trifluoromethyl)phenyl]-5-[(4-carboxyphenyl)methylene]-2-thioxo-4-thiazolidinone (CFTRinh-172)

(2) 3-[(3-trifluoromethyl)phenyl]-5-[(4-nitrophenyl)methylene]-2-thioxo-4-thiazolidinone(CFTRinh-020);

(3) 3-[(3-trifluoromethyl)phenyl]-5-[(4-oxycarboxyphenyl)methylene]-2-thioxo-4-thiazolidinone (CFTRinh-029);

(4) 3-[(3-trifluoromethyl)phenyl]-5-[(3,4-dihydroxyphenyl)methylene]-2-thioxo-4-thiazolidinone (CFTRinh-185),

(5) 3-[(3-trifluoromethyl)phenyl]-5-[(3,5-dibromo-4-hydroxyphenyl)methylene]-2-thioxo-4-thiazolidinone (CFTRinh-214)

(6) 3-[(3-trifluoromethyl)phenyl]-5-[(3-bromo-4-hydroxy-5-nitrophenyl)methylene]-2-thioxo-4-thiazolidinone (CFTRinh-236).

A table of exemplary results is attached.

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Attorney Docket	UCSF-291
First Named Inventor	VERKMAN, ALAN
Application Number	10/676,727
Confirmation No.	2946
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Title: "CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR PROTEIN INHIBITORS AND USES THEREOF"	

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Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 10, 2004

By: _____
Carol L. Francis
Registration No. 36,513

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

To the best of applicant's knowledge, the activity of any of these compounds with respect to cystic fibrosis transmembrane conductance regulator (CFTR) protein was not known prior to the applicant's invention.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: May 10, 2004

By: _____
Carol L. Francis
Registration No. 36,513

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	**10/676,727**
				Filing Date	**September 30, 2003**
				First Named Inventor	**VERKMAN, ALAN**
				Group Art Unit	**1614**
(use as many sheets as necessary)				Examiner Name	**Unassigned**
Sheet	1	of	1	Attorney Docket Number	**UCSF-291**

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Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
		Memorandum Regarding Compound Collections, Dated May 15, 2003	

Examiner Signature		Date Considered	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	1	of	4

Complete if Known	
Application Number	10/676,727
Filing Date	September 30, 2003
Confirmation Number	2946
First Named Inventor	VERKMAN, ALAN
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	UCSF-291

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	U.S. Patent Documents Number	Kind Code[2] (if known)	Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, columns, lines, Where Relevant Passages or Relevant Figures Appear
		4,965,155	B1	Nishiguchi et al.	10/23/1990	
		2002/0049211	A1	Sobolov-Jaynes et al.	04/25/2002	
		2002/0049214	A1	Gibbs et al.	04/25/2002	
		6,380,186	B1	Howard	04/30/2002	
		6,403,592	B1	Howard	06/11/2002	
		2002/0072519	A1	Howard	06/13/2002	
		2002/0091117	A1	Howard	07/11/2002	
		2002/0091118	A1	Howard	07/11/2002	
		2002/0091119	A1	Howard	07/11/2002	
		6,423,708	B1	Gibbs et al.	07/23/2002	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Documents Office[3]	Number[4]	Kind Code[5] (if known)	Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
/		JP	1-156752	A	SEE APPENDIX C (BX)	06/20/1989		
		JP	1-173065	A	SEE APPENDIX C (BX)	07/07/1989		
		JP	1-172836	A	SEE APPENDIX C (BX)	07/07/1989		

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		Abdel-Rahman et al., *"Heterodiene Synthesis I Reaction of 5-Arylidenerhodanine Derivatives with 1-Morpholinocyclohexene Enamine", Synthetic Communications 19(3&4) pgs 345-354 (1989).*	
		Abdel-Rahman et al., *"A Chemical Evidence Supporting the Formation of Dihydropyran Aducts from the Reaction of 5-Arylidenerhodanines with 1-Morpholonocyclohexene through zwitterionic Intermediate ", Afinidad L. 50(445), pgs. 155-159 (1993).*	
		Abdel-Rahman, *"Dihydopyrans form the Heterodienic Reaction of 5-Arylidenerhodanine Derivatives with Isoprene", Chem Papers 47(6) 385-387 (1993).*	
		Cabantchik et al., *"Chemical Probes for Anion Transporters of Mammalian Cell Membranes", Invited Review The American Physiological Society pgs. C803-C827 (1992).*	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 2 of 4

Complete if Known	
Application Number	10/262,573
Filing Date	September 30, 2002
First Named Inventor	VERKMAN, ALAN
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	UCSF-291

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		Edwards et al., *"Induction of a Glibenclamide-sensitive K-current by Modification of a Delayed Rectifier Channel in Rat Portal Vein and Insulinoma Cells" Br. J. Pharmacol.* 110, 1280-1281 (1993).	
		El-Shafei et al., *"Applications of Phase-Transfer Catalysis In Reactions with Rhodanine Derivatives", Gazzetta Chimica Italiana,* 120, pgs. 197-201 (1990).	
		Gabriel et al., *"Cystic Fibrosis Heterozygote Resistance to Cholera Toxin in the Cystic Fibrosis Mouse Model",* Science Volume 266, pgs 107-109 (1994).	
		Gabriel et al., *"A Novel Plant-Derived Inhibitor of cAMP-Mediated Fluid and Chloride Secretion"* The American Physiological Society pgs G58-G63 (1999).	
		Galietta et al., *"Novel CFTR Chloride Channel Activators Identified by Screening of Combinatorial Libraries Based on Flavone and Benzoquinolizinium Lead Compounds",* J. Biological Chemistry Vol 276, No. 23 pp. 19723-19728 (June, 2001)	
		Gorbach et al., *"Acute Undifferentiated Human Dxiarrhea in the Tropics",* The journal of Clinical Investigations" Volume 50, pp. 881-889 (1971).	
		Grubb et al., *"Pathophysiology of Gene-Targeted Mouse Models for Cystic Fibrosis" The American Physiology Society, Physiology Reviews Vol. 79 Suppl. S193-S214 (1999).*	
		Gupta et al., *"Synthesis and Fungitoxicity of Some 5-Substituted-3-Polynitrophenyl Rhodanines",* J. Indian Chem Soc. Vol LV, pp. 483-485. (1978).	
		Hongre et al., *"Effects of Sulphonyllureas on camp-Stimulated Cl- Transport Via the Cytic Fibrosis Gene Product in Human Epithelial Cells",* Pflugers Arch 426: 284-287 (1994).	
		Jayaraman et al., *"Submucosal Gland Secretions in Airways From Cystic Fibrosis Patients Have Normal [Na+] and ph But Elevated Viscosity",* PNAS VO> 98 No.14 8119-8123 (July 2001).	
		Khalil et al., *"The Action of Arllamines on 3-Aryl-5-Arylmethylenerhodanines",* Revue Roumaine de Chimie 23, 6, pp. 935-941 (1978).	
		Khan et al., *"Synthesis and Insecticidal Activity if 5-amino-7-aryl-6-cyano-3-substitute-thiazolo[4,5-b]-2,3,4,7.....",* Indian Journal of Chemistry Vol. 37B pp. 1069-1074 (1998).	
		Ladnaya et al., *"Synthesis and Properties of Thiazolidons-4 Obtained From Phenamine II. Thiasolidindions-2,4",* Luov Medical Institute pp. 37-41	

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 3 of 4

Complete if Known	
Application Number	10/262,573
Filing Date	September 30, 2002
First Named Inventor	VERKMAN, ALAN
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	UCSF-291

OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS

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		Lohi et al., *"Upregulation of CFTR Expression but not SLC26A3 and SLC9A3 in Ulcerative Colitis", American Journal Physio Gastroinest Liver Physiology 283 G567-G575 (2002).*	
		Makhlouf et al., *"New Antomicrobial Rhodanines"* Pharmazie. 51, 430-431 (1996).	
		McDonough et al., *"Novel Pore-Lining Residues in CFTR That Govern Permeation and Open-Channel Block"*, Neuron Volume 13, pgs 623-634 (September, 1994).	
		Noone et al., *"CFTR-Opathies':Disease Phenotypes Associated with Cystic Fibrosis Transmembrane Regualtor Gene Mutations"* Respir Res. 2:328-332 (2001).	
		Oi et al., *"Identification in Traditional herbal Medications and Confirmation by Synthesis of Factors that Inhibit Cholera Toxin-Induced Fluid Accumulation"*, PNAS Vol. 99 No. 5 3042-3046 (March, 2002).	
		Omar et al., *"The Role of Substituents at Position03 on the Mode of Cleavage of 5-Arylmethylene-2, 4-dioxothiazolidines"*, Journal f. prakt. Chemie. Band 331, Heft 3, 1989, S393-S398 (1989).	
		Pilewski et al., *"Role of CFTR in Airway Disease" Physiological Reviews Vol 79, Suppl No.1, pgs. S215-S255 (January, 1999).*	
		Rabe et al., *"Cl- Channel Inhibition by Glibenclamide is Not Specific for the CFTR-type Cl- Channel"*, Pflugers Arch-Eur J. Physiol 429: 659-662 (1995).	
		Rasola et al., *"Volume-Sensitive Chloride Currents in Four Epithelial Cell Lines Are Not Directly Correlated to the Expression of the MDR-1 Gene"*, The J. Biol Chem. Vol. 269, No.2 pp. 1432-1436 (Jan. 1994).	
		Richardson et al., *"Studies on the Genetic and Cellular Control of Sensitivity to Enterotoxins in the Sealed Adult Mouse Model"*, Infection and Immunity Vol. 54, No. 2, pp. 522-528 (Nov. 1986).	
		Schultz et al., *"Pharmacology of CFTR Chloride Channel Activity", Physiological Reviews Vol 79, Suppl No.1, pgs. S109—S144 (January, 1999).*	
		Sheppard et al., *"Effect of ATP-sensitive K+ Channel regulators on Cystic Fibrosis Transmembrane Conductance Regulator Chloride Currents"*, J. Gen Physiol. Pp. 573-591 (October 1992).	
		Tejchman et al., *"Introduction of Selenium to Hetreocyclic Compounds. Part VII. Synthesis of 3-Alkyl-5-5-benzylidene- and ....."*, Polish j. Chem., 73, 1315-1322 (1999).	

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Sheet 4 of 4

Complete if Known	
Application Number	10/262,573
Filing Date	September 30, 2002
First Named Inventor	VERKMAN, ALAN
Group Art Unit	1614
Examiner Name	Unassigned
Attorney Docket Number	UCSF-291

OTHER PRIOR ART—NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T[2]
		Tejchman et al., *"Introduction of Selenium to Hetreocyclic Compounds. Part VI. Synthesis of 3-Aryl-5-benzylidene- and ....."*, Polish j. Chem., 70, 1124-1134 (1996).	
		Tiwari et al., *"Synthesis and Fungiicidal Activity of Some 3,7-diaryl-6-cyanorhodanino[4,5-b]-pyridin-5....."*, Indian Journal of Chemistry Vol. 28B pp. 796-798 (1989).	
		Wong et al., *"CFTR Gene and Male Fertility"*, Molecular Human Reproduction Vol. 4, No. 2 pp. 107-110 (1998).	
		Yadav et al., *"Synthesis and Fungitoxicity of Rationally Designed Thiazolo-1,3-dithiins, -thiazines , and oxathiins"* J. Agric. Food Chem 40, pp. 1214-126 (1992).	
		Yamada et al., *"Dai-2-bu", Utsunomiya Daigaku Kyoikugakubu Kiyo"*,34:33-41 (1983).	
		Yamazaki et al., *"Inhibitory Effects of Glibenclamide on Cystic Fibrosis Transmembrane Regulator, Swelling-Activated, and Ca^{2+}-Activated Cl- Channels in Mammalian Cardiac Myocytes"* Circulation Research Vo. 81(1) pp. 101-109. (July 1997).	
		Appendix C – Thiazolidinone Chemical Structure Search (Identified Refereņces) Pages 1-70 (2002).	

Examiner Signature		Date Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]Unique citation designation number. [2]Applicant is to place a check mark here if English language Translation is attached.